Appendix C – Additional results

Table of contents

Additional results for primary analyses

Table C1. Pair-wise comparisons for ACR50 response: MTX-naïve

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	IM/sc MTX+ADA	MTX+CTZ	MTX+ETN	MTX+GOL (sc)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+CyA	IM/sc MTX+CyA	MTX+HCQ/CQ	MTX+SSZ	MTX+SSZ+HCQ
MTX+ABAT (IV)	1.8 (1.0 to 3.4) 98%	--																
MTX+ABAT (sc)	2.0 (0.94 to 4.0) 97%	1.1 (0.40 to 2.7) 56%	--															
MTX+ADA	2.1 (1.5 to 2.9) >99%	1.1 (0.57 to 2.2) 67%	1.1 (0.49 to 2.4) 56%	--														
IM/sc MTX+ADA	2.2 (0.80 to 6.1) 94%	1.2 (0.37 to 4.0) 63%	1.1 (0.33 to 3.8) 57%	1.1 (0.37 to 3.1) 54%	--													
MTX+CTZ	1.5 (0.83 to 2.7) 93%	0.80 (0.35 to 1.9) 27%	0.75 (0.30 to 1.9) 26%	0.71 (0.36 to 1.4) 13%	0.68 (0.21 to 2.2) 23%	--												
MTX+ETN	3.0 (2.0 to 4.6) >99%	1.6 (0.78 to 3.5) 92%	1.5 (0.69 to 3.5) 86%	1.4 (0.86 to 2.4) 93%	1.4 (0.46 to 4.1) 72%	2.0 (1.00 to 4.1) 97%	--											
MTX+GOL (sc)	1.3 (0.68 to 2.6) 83%	0.72 (0.30 to 1.8) 21%	0.68 (0.25 to 1.8) 21%	0.63 (0.30 to 1.3) 10%	0.61 (0.18 to 2.0) 19%	0.90 (0.37 to 2.2) 38%	0.45 (0.20 to 0.95) 2%	--										
MTX+IFX	2.0 (1.3 to 3.8) >99%	1.1 (0.54 to 2.7) 62%	1.0 (0.45 to 2.7) 53%	0.97 (0.57 to 2.0) 45%	0.92 (0.32 to 3.0) 43%	1.4 (0.68 to 3.3) 83%	0.68 (0.37 to 1.4) 12%	1.5 (0.70 to 3.9) 87%	--									
MTX+RTX	2.4 (1.3 to 4.4) 99%	1.3 (0.55 to 3.1) 76%	1.2 (0.48 to 3.2) 67%	1.1 (0.57 to 2.3) 68%	1.1 (0.34 to 3.6) 56%	1.6 (0.69 to 3.7) 90%	0.81 (0.37 to 1.7) 25%	1.8 (0.73 to 4.5) 92%	1.2 (0.48 to 2.4) 68%	--								
MTX+TCZ (4 mg/kg)	1.7 (0.95 to 2.9) 97%	0.90 (0.39 to 2.1) 37%	0.84 (0.34 to 2.1) 34%	0.79 (0.42 to 1.5) 19%	0.74 (0.23 to 2.4) 29%	1.1 (0.50 to 2.5) 62%	0.55 (0.27 to 1.1) 4%	1.2 (0.52 to 3.0) 72%	0.81 (0.35 to 1.6) 25%	0.68 (0.30 to 1.6) 15%	--							
MTX+TCZ (8 mg/kg)	1.9 (1.1 to 3.4) 98%	1.0 (0.45 to 2.4) 54%	0.96 (0.39 to 2.4) 46%	0.91 (0.48 to 1.7) 36%	0.86 (0.27 to 2.8) 39%	1.3 (0.57 to 2.9) 76%	0.64 (0.32 to 1.3) 8%	1.4 (0.60 to 3.5) 82%	0.94 (0.39 to 1.9) 42%	0.79 (0.35 to 1.8) 26%	1.2 (0.63 to 2.1) 72%	--						
MTX+TOFA	3.0 (1.0 to 9.4) 98%	1.7 (0.48 to 5.9) 80%	1.6 (0.42 to 5.7) 75%	1.4 (0.47 to 4.6) 74%	1.4 (0.32 to 6.1) 67%	2.0 (0.60 to 7.4) 88%	1.0 (0.32 to 3.3) 51%	2.2 (0.66 to 8.4) 91%	1.5 (0.43 to 4.9) 74%	1.3 (0.38 to 4.5) 64%	1.8 (0.55 to 6.4) 86%	1.6 (0.48 to 5.5) 78%	--					
MTX+CyA	1.7 (0.86 to 3.4) 94%	0.93 (0.37 to 2.3) 43%	0.88 (0.33 to 2.3) 39%	0.81 (0.39 to 1.7) 29%	0.79 (0.23 to 2.7) 34%	1.2 (0.48 to 2.8) 64%	0.58 (0.26 to 1.2) 7%	1.3 (0.50 to 3.3) 72%	0.83 (0.33 to 1.9) 33%	0.71 (0.29 to 1.8) 22%	1.0 (0.43 to 2.5) 54%	0.90 (0.37 to 2.1) 40%	0.56 (0.15 to 2.0) 18%	--				
IM/sc MTX+CyA	1.6 (0.45 to 6.0) 75%	0.84 (0.21 to 3.8) 41%	0.79 (0.19 to 3.8) 37%	0.75 (0.21 to 3.0) 34%	0.70 (0.19 to 2.9) 30%	1.0 (0.26 to 4.6) 52%	0.52 (0.14 to 2.2) 17%	1.2 (0.28 to 5.6) 59%	0.76 (0.19 to 3.2) 35%	0.65 (0.16 to 2.8) 28%	0.96 (0.24 to 4.1) 48%	0.83 (0.21 to 3.6) 39%	0.52 (0.10 to 2.8) 22%	0.92 (0.22 to 4.2) 46%	--			
MTX+HCQ/CQ	0.78 (0.23 to 2.9) 35%	0.43 (0.10 to 1.8) 11%	0.40 (0.10 to 1.8) 10%	0.37 (0.11 to 1.4) 7%	0.35 (0.07 to 1.8) 10%	0.52 (0.14 to 2.2) 18%	0.26 (0.08 to 0.93) 2%	0.59 (0.15 to 2.6) 23%	0.38 (0.10 to 1.5) 8%	0.33 (0.08 to 1.4) 6%	0.47 (0.13 to 1.9) 14%	0.41 (0.11 to 1.7) 10%	0.26 (0.05 to 1.5) 6%	0.47 (0.11 to 1.9) 13%	0.50 (0.08 to 3.0) 22%	--		
MTX+SSZ	1.1 (0.41 to 2.8) 57%	0.59 (0.19 to 1.8) 17%	0.56 (0.17 to 1.8) 15%	0.52 (0.19 to 1.4) 9%	0.50 (0.13 to 1.9) 15%	0.74 (0.24 to 2.2) 28%	0.36 (0.14 to 0.94) 2%	0.82 (0.25 to 2.6) 37%	0.53 (0.17 to 1.5) 11%	0.46 (0.14 to 1.4) 8%	0.67 (0.22 to 1.9) 22%	0.58 (0.19 to 1.7) 15%	0.36 (0.09 to 1.4) 7%	0.64 (0.20 to 2.0) 20%	0.67 (0.14 to 3.2) 32%	1.4 (0.43 to 4.5) 70%	--	
MTX+SSZ+HCQ	2.3 (1.2 to 4.8) 99%	1.3 (0.49 to 3.3) 71%	1.2 (0.44 to 3.3) 64%	1.1 (0.52 to 2.5) 61%	1.1 (0.31 to 3.8) 54%	1.5 (0.64 to 4.0) 86%	0.77 (0.43 to 1.5) 19%	1.7 (0.68 to 4.7) 89%	1.1 (0.44 to 2.6) 62%	0.96 (0.39 to 2.5) 46%	1.4 (0.58 to 3.5) 79%	1.2 (0.50 to 3.1) 68%	0.74 (0.21 to 2.9) 33%	1.3 (0.54 to 3.7) 74%	1.5 (0.33 to 6.3) 69%	3.0 (0.93 to 8.9) 97%	2.2 (0.85 to 5.6) 95%	--
IM/sc MTX	1.1 (0.59 to 2.2) 65%	0.61 (0.25 to 1.5) 12%	0.57 (0.22 to 1.5) 11%	0.54 (0.27 to 1.1) 4%	0.51 (0.24 to 1.1) 4%	0.75 (0.32 to 1.8) 24%	0.38 (0.17 to 0.80) 1%	0.84 (0.33 to 2.2) 35%	0.55 (0.22 to 1.2) 5%	0.47 (0.19 to 1.1) 4%	0.69 (0.28 to 1.6) 16%	0.59 (0.25 to 1.4) 9%	0.37 (0.11 to 1.3) 6%	0.66 (0.26 to 1.7) 18%	0.72 (0.22 to 2.1) 28%	1.4 (0.33 to 5.8) 70%	1.0 (0.33 to 3.2) 53%	0.49 (0.18 to 1.3) 6%

Treatment effects are presented as the median Odds Ratio (OR) with 95% credible intervals and the probability of superiority (higher odds of ACR50 response) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; CQ, chloroquine; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C2. Treatment rankings for ACR50 response: MTX-naïve

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 20=worst) median (95%CrI)
MTX+TOFA	36.96	3 (1 to 16)
MTX+ETN	17.79	3 (1 to 8)
IM/sc MTX+ADA	12.55	6 (1 to 17)
IM/sc MTX+CyA	7.86	12 (1 to 19)
MTX+RTX	7.11	5 (1 to 14)
MTX+SSZ+HCQ	6.62	6 (1 to 15)
MTX+ABAT (sc)	3.26	8 (1 to 17)
MTX+IFX	1.99	8 (2 to 15)
MTX+ABAT (IV)	1.55	9 (2 to 17)
MTX+CyA	1.26	11 (2 to 18)
MTX+TCZ (8 mg/kg)	1.07	9 (2 to 16)
MTX+HCQ/CQ	0.45	18 (4 to 19)
MTX+TCZ (4 mg/kg)	0.38	11 (4 to 17)
MTX+ADA	0.34	7 (3 to 13)
MTX+SSZ	0.30	16 (4 to 19)
MTX+CTZ	0.27	13 (4 to 18)
MTX+GOL (sc)	0.25	14 (5 to 19)
MTX	<0.01	17 (14 to 19)
IM/sc MTX	<0.01	16 (8 to 19)

Abbreviations: ABAT, abatacept; ADA, adalimumab; CQ, chloroquine; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C3. Pair-wise comparisons for radiographic progression (change from baseline, random-effects model): MTX-naïve

Medication	MTX	MTX+ABAT (IV)	MTX+ADA	MTX+CTZ	MTX+ETN	MTX+GOL (sc)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+CyA
MTX+ABAT (IV)	-0.20 (-0.60 to 0.19) 88%	--										
MTX+ADA	-0.37 (-0.64 to -0.08) 99%	-0.17 (-0.64 to 0.34) 79%	--									
MTX+CTZ	-0.39 (-0.68 to -0.10) 99%	-0.18 (-0.66 to 0.32) 81%	-0.02 (-0.43 to 0.37) 54%	--								
MTX+ETN	-0.37 (-0.59 to -0.11) 99%	-0.17 (-0.61 to 0.33) 79%	0.00 (-0.36 to 0.37) 49%	0.02 (-0.34 to 0.41) 45%	--							
MTX+GOL (sc)	-0.13 (-0.53 to 0.29) 76%	0.08 (-0.49 to 0.66) 37%	0.25 (-0.27 to 0.74) 14%	0.26 (-0.24 to 0.77) 13%	0.24 (-0.25 to 0.71) 13%	--						
MTX+IFX	-0.43 (-0.82 to -0.04) 98%	-0.23 (-0.78 to 0.33) 83%	-0.06 (-0.55 to 0.40) 62%	-0.04 (-0.53 to 0.44) 58%	-0.06 (-0.55 to 0.38) 63%	-0.30 (-0.87 to 0.26) 89%	--					
MTX+RTX	-0.38 (-0.79 to 0.01) 97%	-0.18 (-0.74 to 0.39) 77%	-0.01 (-0.52 to 0.47) 52%	0.01 (-0.49 to 0.50) 49%	-0.01 (-0.50 to 0.43) 53%	-0.26 (-0.84 to 0.32) 85%	0.05 (-0.52 to 0.61) 41%	--				
MTX+TCZ (4 mg/kg)	-0.25 (-0.66 to 0.16) 91%	-0.04 (-0.62 to 0.53) 57%	0.12 (-0.39 to 0.61) 29%	0.14 (-0.37 to 0.64) 26%	0.12 (-0.38 to 0.57) 28%	-0.12 (-0.70 to 0.46) 70%	0.18 (-0.38 to 0.75) 23%	0.13 (-0.44 to 0.70) 29%	--			
MTX+TCZ (8 mg/kg)	-0.37 (-0.77 to 0.03) 97%	-0.16 (-0.73 to 0.40) 75%	0.01 (-0.50 to 0.48) 49%	0.02 (-0.47 to 0.51) 45%	0.00 (-0.49 to 0.45) 49%	-0.24 (-0.82 to 0.33) 83%	0.06 (-0.50 to 0.61) 39%	0.02 (-0.55 to 0.58) 47%	-0.12 (-0.50 to 0.26) 77%	--		
MTX+TOFA	-0.21 (-0.85 to 0.47) 73%	-0.01 (-0.76 to 0.77) 51%	0.16 (-0.54 to 0.89) 33%	0.18 (-0.53 to 0.93) 31%	0.16 (-0.54 to 0.87) 33%	-0.08 (-0.86 to 0.72) 58%	0.22 (-0.52 to 1.00) 27%	0.18 (-0.58 to 0.97) 33%	0.05 (-0.71 to 0.83) 45%	0.16 (-0.60 to 0.94) 34%	--	
MTX+CyA	-0.21 (-0.50 to 0.10) 92%	-0.01 (-0.49 to 0.50) 51%	0.16 (-0.25 to 0.57) 19%	0.18 (-0.24 to 0.60) 17%	0.16 (-0.24 to 0.53) 18%	-0.08 (-0.59 to 0.44) 64%	0.22 (-0.27 to 0.72) 15%	0.17 (-0.32 to 0.69) 21%	0.04 (-0.46 to 0.56) 43%	0.15 (-0.33 to 0.67) 23%	-0.00 (-0.74 to 0.71) 51%	--
MTX+SSZ+HCQ	-0.03 (-0.75 to 0.72) 54%	0.17 (-0.65 to 1.0) 34%	0.34 (-0.43 to 1.1) 19%	0.35 (-0.41 to 1.2) 18%	0.33 (-0.36 to 1.1) 17%	0.10 (-0.73 to 0.95) 41%	0.40 (-0.42 to 1.3) 17%	0.35 (-0.46 to 1.2) 19%	0.21 (-0.60 to 1.1) 30%	0.33 (-0.47 to 1.2) 21%	0.17 (-0.83 to 1.2) 36%	0.18 (-0.61 to 0.98) 33%

Treatment effects are presented as the median standardized mean difference (smd) with 95% credible intervals and the probability of superiority (less radiographic progression) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; RTX, rituximab; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C4. Treatment rankings for radiographic progression (change from baseline, random-effects model): MTX-naïve

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 13=worst) median (95%CrI)
MTX+IFX	22.45	3 (1 to 11)
MTX+RTX	14.60	4 (1 to 11)
MTX+TOFA	13.60	9 (1 to 13)
MTX+TCZ (8 mg/kg)	11.89	5 (1 to 11)
MTX+CTZ	10.36	4 (1 to 10)
MTX+ADA	7.78	5 (1 to 10)
MTX+SSZ+HCQ	6.45	11 (1 to 13)
MTX+ETN	5.13	5 (1 to 10)
MTX+TCZ (4 mg/kg)	2.97	8 (1 to 13)
MTX+ABAT (IV)	2.53	9 (1 to 13)
MTX+GOL (sc)	1.25	10 (2 to 13)
MTX+CyA	1.00	9 (2 to 12)
MTX	<0.01	12 (9 to 13)

Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; RTX, rituximab; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C5. Pair-wise comparisons for radiographic progression (change from baseline, fixed-effects model): MTX-naïve

Medication	MTX	MTX+ABAT (IV)	MTX+ADA	MTX+CTZ	MTX+ETN	MTX+GOL (sc)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+CyA
MTX+ABAT (IV)	-0.20 (-0.38 to -0.03) 99%	--										
MTX+ADA	-0.40 (-0.53 to -0.26) >99%	-0.19 (-0.42 to 0.03) 95%	--									
MTX+CTZ	-0.39 (-0.55 to -0.24) >99%	-0.19 (-0.42 to 0.05) 94%	0.01 (-0.20 to 0.21) 48%	--								
MTX+ETN	-0.40 (-0.51 to -0.29) >99%	-0.19 (-0.40 to 0.01) 97%	-0.00 (-0.17 to 0.18) 50%	-0.00 (-0.19 to 0.18) 52%	--							
MTX+GOL (sc)	-0.13 (-0.35 to 0.09) 88%	0.07 (-0.21 to 0.35) 30%	0.27 (0.01 to 0.52) 2%	0.26 (-0.01 to 0.53) 3%	0.27 (0.02 to 0.51) 2%	--						
MTX+IFX	-0.43 (-0.59 to -0.26) >99%	-0.22 (-0.46 to 0.02) 96%	-0.03 (-0.24 to 0.19) 61%	-0.03 (-0.26 to 0.19) 62%	-0.03 (-0.23 to 0.17) 61%	-0.29 (-0.57 to -0.02) 98%	--					
MTX+RTX	-0.39 (-0.57 to -0.20) >99%	-0.18 (-0.43 to 0.07) 92%	0.01 (-0.21 to 0.24) 47%	0.01 (-0.23 to 0.24) 48%	0.01 (-0.20 to 0.22) 46%	-0.26 (-0.54 to 0.03) 96%	0.04 (-0.21 to 0.28) 37%	--				
MTX+TCZ (4 mg/kg)	-0.25 (-0.46 to -0.03) 99%	-0.04 (-0.32 to 0.24) 62%	0.15 (-0.11 to 0.41) 13%	0.15 (-0.13 to 0.41) 14%	0.15 (-0.09 to 0.39) 11%	-0.12 (-0.42 to 0.19) 77%	0.18 (-0.09 to 0.45) 10%	0.14 (-0.14 to 0.42) 16%	--			
MTX+TCZ (8 mg/kg)	-0.36 (-0.56 to -0.16) >99%	-0.16 (-0.42 to 0.10) 88%	0.04 (-0.21 to 0.28) 38%	0.03 (-0.23 to 0.28) 40%	0.04 (-0.19 to 0.26) 37%	-0.23 (-0.52 to 0.06) 94%	0.06 (-0.19 to 0.32) 31%	0.03 (-0.24 to 0.29) 43%	-0.11 (-0.26 to 0.03) 94%	--		
MTX+TOFA	-0.20 (-0.76 to 0.37) 76%	0.00 (-0.59 to 0.60) 49%	0.20 (-0.39 to 0.78) 25%	0.19 (-0.40 to 0.78) 26%	0.20 (-0.38 to 0.78) 25%	-0.07 (-0.68 to 0.54) 59%	0.23 (-0.36 to 0.82) 23%	0.19 (-0.41 to 0.78) 27%	0.05 (-0.55 to 0.66) 44%	0.16 (-0.43 to 0.76) 30%	--	
MTX+CyA	-0.23 (-0.39 to -0.07) >99%	-0.03 (-0.26 to 0.21) 58%	0.17 (-0.04 to 0.38) 6%	0.16 (-0.06 to 0.38) 7%	0.17 (-0.03 to 0.36) 5%	-0.10 (-0.37 to 0.17) 76%	0.20 (-0.03 to 0.43) 4%	0.16 (-0.08 to 0.40) 10%	0.02 (-0.25 to 0.28) 45%	0.13 (-0.12 to 0.38) 15%	-0.03 (-0.62 to 0.56) 54%	--
MTX+SSZ+HCQ	-0.05 (-0.68 to 0.59) 56%	0.15 (-0.51 to 0.81) 32%	0.34 (-0.30 to 0.99) 15%	0.34 (-0.31 to 1.00) 15%	0.34 (-0.28 to 0.98) 14%	0.08 (-0.59 to 0.76) 41%	0.37 (-0.28 to 1.0) 13%	0.33 (-0.32 to 1.00) 16%	0.20 (-0.48 to 0.86) 28%	0.31 (-0.36 to 0.97) 18%	0.14 (-0.70 to 1.00) 37%	0.18 (-0.48 to 0.84) 30%

Treatment effects are presented as the median standardized mean difference (smd) with 95% credible intervals and the probability of superiority (less radiographic progression) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; RTX, rituximab; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C6. Pair-wise comparisons for withdrawals due to adverse events: MTX-naïve

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	IM/sc MTX+ADA	MTX+ETN	MTX+GOL (sc)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+AZA	MTX+CyA	IM/sc MTX+CyA	MTX+HCQ/CQ	MTX+SSZ	MTX+SSZ+HCQ
MTX+ABAT (IV)	0.70 (0.21 to 2.3) 74%	--																
MTX+ABAT (sc)	0.97 (0.20 to 4.9) 52%	1.4 (0.19 to 10) 36%	--															
MTX+ADA	1.2 (0.63 to 2.2) 24%	1.7 (0.43 to 6.6) 19%	1.2 (0.22 to 6.7) 38%	--														
IM/sc MTX+ADA	0.81 (0.07 to 8.1) 58%	1.2 (0.07 to 15) 46%	0.84 (0.04 to 14) 55%	0.67 (0.05 to 7.4) 64%	--													
MTX+ETN	0.80 (0.45 to 1.6) 77%	1.1 (0.31 to 4.8) 42%	0.84 (0.15 to 4.7) 59%	0.66 (0.29 to 1.8) 83%	1.0 (0.09 to 14) 50%	--												
MTX+GOL (sc)	2.4 (0.67 to 9.7) 8%	3.4 (0.59 to 21) 8%	2.5 (0.31 to 20) 18%	1.9 (0.49 to 9.2) 15%	2.9 (0.21 to 48) 20%	2.9 (0.67 to 13) 6%	--											
MTX+IFX	2.5 (0.94 to 7.8) 3%	3.6 (0.75 to 18) 5%	2.6 (0.40 to 18) 14%	2.1 (0.68 to 7.6) 9%	3.1 (0.27 to 49) 17%	3.2 (0.95 to 11) 3%	1.1 (0.20 to 5.7) 46%	--										
MTX+RTX	0.83 (0.22 to 3.0) 62%	1.2 (0.20 to 6.8) 42%	0.86 (0.11 to 6.4) 56%	0.68 (0.16 to 2.9) 71%	1.0 (0.07 to 17) 49%	1.0 (0.23 to 4.2) 48%	0.35 (0.05 to 2.2) 89%	0.32 (0.06 to 1.6) 92%	--									
MTX+TCZ (4 mg/kg)	1.3 (0.46 to 3.8) 25%	1.9 (0.39 to 9.4) 19%	1.4 (0.21 to 8.9) 36%	1.1 (0.34 to 3.8) 43%	1.7 (0.13 to 24) 34%	1.7 (0.46 to 5.3) 18%	0.56 (0.10 to 2.9) 77%	0.52 (0.12 to 2.2) 84%	1.6 (0.30 to 8.5) 26%	--								
MTX+TCZ (8 mg/kg)	2.3 (0.82 to 6.4) 5%	3.2 (0.66 to 16) 6%	2.4 (0.35 to 15) 17%	1.9 (0.59 to 6.5) 12%	2.8 (0.23 to 42) 19%	2.8 (0.81 to 9.0) 4%	0.97 (0.17 to 4.9) 52%	0.90 (0.20 to 3.7) 57%	2.7 (0.54 to 14) 9%	1.7 (0.58 to 5.0) 12%	--							
MTX+TOFA	0.90 (0.17 to 4.6) 55%	1.3 (0.16 to 10) 41%	0.92 (0.09 to 9.1) 53%	0.74 (0.13 to 4.4) 63%	1.1 (0.06 to 23) 47%	1.1 (0.18 to 6.4) 45%	0.38 (0.04 to 3.0) 83%	0.35 (0.05 to 2.4) 86%	1.1 (0.13 to 8.8) 47%	0.67 (0.10 to 4.8) 66%	0.39 (0.06 to 2.7) 84%	--						
MTX+AZA	5.8 (1.6 to 24) 1%	8.3 (1.4 to 52) 1%	5.9 (0.75 to 53) 4%	4.8 (1.2 to 23) 2%	7.2 (0.54 to 125) 6%	7.2 (1.6 to 33) 1%	2.5 (0.37 to 16) 15%	2.2 (0.39 to 14) 16%	7.1 (1.2 to 48) 2%	4.4 (0.81 to 25) 4%	2.6 (0.49 to 14) 12%	6.6 (0.77 to 58) 4%	--					
MTX+CyA	1.1 (0.37 to 2.4) 44%	1.5 (0.29 to 6.3) 28%	1.1 (0.16 to 6.1) 46%	0.87 (0.27 to 2.5) 63%	1.3 (0.10 to 18) 41%	1.3 (0.35 to 3.5) 30%	0.45 (0.08 to 1.9) 88%	0.41 (0.09 to 1.4) 93%	1.3 (0.23 to 5.8) 38%	0.79 (0.18 to 2.8) 66%	0.46 (0.10 to 1.6) 91%	1.2 (0.17 to 7.0) 44%	0.18 (0.03 to 0.82) 99%	--				
IM/sc MTX+CyA	8.9 (0.98 to 139) 3%	13 (1.0 to 258) 2%	9.5 (0.58 to 224) 6%	7.3 (0.76 to 127) 4%	11 (0.79 to 267) 4%	11 (1.1 to 184) 2%	3.8 (0.27 to 79) 16%	3.5 (0.29 to 63) 15%	11 (0.86 to 229) 3%	6.7 (0.57 to 130) 6%	3.9 (0.33 to 75) 13%	10 (0.60 to 242) 5%	1.6 (0.11 to 30) 36%	8.7 (0.84 to 166) 3%	--			
MTX+HCQ/CQ	1.4 (0.40 to 5.3) 30%	1.9 (0.35 to 12) 21%	1.4 (0.19 to 12) 36%	1.1 (0.29 to 5.1) 43%	1.7 (0.12 to 28) 34%	1.7 (0.43 to 7.1) 22%	0.57 (0.09 to 3.8) 74%	0.54 (0.10 to 2.9) 79%	1.6 (0.28 to 11) 28%	1.0 (0.21 to 5.9) 49%	0.60 (0.12 to 3.3) 75%	1.6 (0.19 to 13) 34%	0.23 (0.03 to 1.5) 94%	1.3 (0.30 to 7.5) 36%	0.15 (0.01 to 2.0) 93%	--		
MTX+SSZ	1.3 (0.67 to 2.8) 21%	1.9 (0.48 to 7.8) 16%	1.3 (0.24 to 7.9) 37%	1.1 (0.47 to 3.0) 44%	1.6 (0.15 to 23) 33%	1.6 (0.65 to 4.0) 13%	0.55 (0.12 to 2.5) 80%	0.51 (0.14 to 1.8) 86%	1.6 (0.39 to 7.2) 26%	0.97 (0.29 to 3.7) 52%	0.57 (0.18 to 2.1) 84%	1.5 (0.26 to 9.1) 33%	0.23 (0.05 to 1.0) 97%	1.2 (0.45 to 4.8) 34%	0.15 (0.01 to 1.5) 95%	0.96 (0.26 to 3.4) 53%	--	
MTX+SSZ+HCQ	0.67 (0.28 to 1.5) 84%	0.96 (0.21 to 4.1) 53%	0.69 (0.11 to 4.0) 67%	0.55 (0.19 to 1.6) 88%	0.83 (0.07 to 11) 56%	0.83 (0.31 to 1.9) 67%	0.29 (0.05 to 1.3) 96%	0.26 (0.06 to 0.91) 98%	0.80 (0.17 to 3.8) 62%	0.51 (0.13 to 1.9) 87%	0.30 (0.07 to 1.1) 97%	0.74 (0.11 to 4.7) 62%	0.11 (0.02 to 0.52) >99%	0.64 (0.20 to 2.3) 77%	0.07 (0.00 to 0.79) 98%	0.49 (0.12 to 1.8) 86%	0.51 (0.18 to 1.3) 93%	--
IM/sc MTX	1.9 (0.56 to 6.7) 14%	2.7 (0.49 to 15) 11%	1.9 (0.25 to 14) 25%	1.5 (0.41 to 6.7) 26%	2.3 (0.32 to 20) 19%	2.3 (0.55 to 9.2) 11%	0.79 (0.12 to 4.6) 62%	0.74 (0.14 to 3.6) 66%	2.2 (0.38 to 14) 17%	1.4 (0.28 to 7.4) 32%	0.81 (0.16 to 4.1) 61%	2.0 (0.25 to 17) 23%	0.32 (0.05 to 2.0) 91%	1.7 (0.43 to 9.6) 20%	0.21 (0.02 to 1.3) 96%	1.4 (0.22 to 7.6) 35%	1.4 (0.34 to 5.8) 30%	2.8 (0.65 to 13) 8%

Treatment effects are presented as the median Rate Ratio (RR) with 95% credible intervals and the probability of superiority (lower odds of withdrawal) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; AZA, azathioprine; CTZ, certolizumab; CQ, chloroquine; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C7. Treatment rankings for withdrawals due to adverse events: MTX-naïve

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 19=worst) median (95%CrI)
IM/sc MTX+ADA	28.82	4 (1 to 18)
MTX+ABAT (IV)	14.27	4 (1 to 15)
MTX+TOFA	13.78	6 (1 to 18)
MTX+SSZ+HCQ	12.55	4 (1 to 12)
MTX+ABAT (sc)	10.9	7 (1 to 18)
MTX+RTX	9.94	6 (1 to 16)
MTX+CyA	2.66	8 (1 to 15)
MTX+ETN	2.57	5 (1 to 13)
MTX+HCQ/CQ	2.01	11 (2 to 18)
MTX+TCZ (4 mg/kg)	1.11	11 (2 to 17)
MTX+GOL (sc)	0.41	15 (4 to 19)
MTX+ADA	0.26	10 (3 to 15)
IM/sc MTX	0.21	13 (3 to 18)
IM/sc MTX+CyA	0.20	19 (7 to 19)
MTX+TCZ (8 mg/kg)	0.13	15 (6 to 18)
MTX+SSZ	0.10	11 (4 to 16)
MTX+IFX	0.07	16 (7 to 19)
MTX+AZA	0.01	18 (12 to 19)
MTX	<0.01	7 (4 to 11)

Abbreviations: ABAT, abatacept; ADA, adalimumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; RTX, rituximab; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C8. Pair-wise comparisons for ACR50 response: MTX-inadequate response

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	MTX+ETN	MTX+GOL (sc)	MTX+GOL (IV)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+HCQ/CQ	MTX+IMGold	MTX+LEF	MTX+SSZ
MTX+ABAT (IV)	3.8 (2.8 to 5.3) >99%	--														
MTX+ABAT (sc)	4.2 (2.7 to 6.5) >99%	1.1 (0.75 to 1.6) 69%	--													
MTX+ADA	4.4 (3.4 to 5.9) >99%	1.1 (0.79 to 1.7) 77%	1.0 (0.68 to 1.6) 60%	--												
MTX+ETN	12 (5.8 to 31) >99%	3.2 (1.5 to 8.5) >99%	2.9 (1.3 to 8.2) 99%	2.8 (1.3 to 7.3) 99%	--											
MTX+GOL (sc)	4.5 (2.6 to 8.0) >99%	1.2 (0.62 to 2.3) 69%	1.1 (0.53 to 2.2) 58%	1.0 (0.55 to 1.9) 53%	0.37 (0.13 to 0.93) 2%	--										
MTX+GOL (IV)	3.6 (1.8 to 7.2) >99%	0.94 (0.43 to 2.0) 43%	0.86 (0.37 to 1.9) 35%	0.83 (0.38 to 1.7) 29%	0.29 (0.09 to 0.79) 1%	0.79 (0.32 to 1.9) 31%	--									
MTX+IFX	3.5 (2.5 to 5.0) >99%	0.91 (0.58 to 1.4) 32%	0.83 (0.48 to 1.4) 23%	0.79 (0.50 to 1.2) 14%	0.28 (0.11 to 0.64) <1%	0.78 (0.39 to 1.5) 22%	0.97 (0.44 to 2.1) 47%	--								
MTX+RTX	3.6 (2.2 to 6.3) >99%	0.93 (0.52 to 1.8) 42%	0.86 (0.44 to 1.8) 33%	0.82 (0.46 to 1.5) 25%	0.30 (0.11 to 0.70) <1%	0.80 (0.38 to 1.8) 29%	1.00 (0.43 to 2.5) 50%	1.0 (0.56 to 2.0) 54%	--							
MTX+TCZ (4 mg/kg)	2.6 (1.4 to 4.6) >99%	0.67 (0.34 to 1.3) 12%	0.62 (0.29 to 1.2) 9%	0.59 (0.30 to 1.1) 5%	0.21 (0.07 to 0.59) <1%	0.58 (0.25 to 1.3) 8%	0.72 (0.28 to 1.7) 24%	0.74 (0.37 to 1.4) 19%	0.71 (0.31 to 1.6) 20%	--						
MTX+TCZ (8 mg/kg)	4.2 (2.5 to 6.8) >99%	1.1 (0.58 to 2.0) 61%	1.0 (0.50 to 1.9) 50%	0.95 (0.51 to 1.7) 43%	0.34 (0.12 to 0.89) 1%	0.93 (0.42 to 1.9) 42%	1.2 (0.47 to 2.7) 64%	1.2 (0.63 to 2.2) 72%	1.1 (0.53 to 2.4) 65%	1.6 (0.96 to 2.7) 97%	--					
MTX+TOFA	5.4 (3.3 to 9.0) >99%	1.4 (0.80 to 2.5) 89%	1.3 (0.69 to 2.4) 81%	1.2 (0.74 to 2.1) 81%	0.44 (0.16 to 1.1) 4%	1.2 (0.56 to 2.6) 70%	1.5 (0.64 to 3.5) 85%	1.6 (0.85 to 2.9) 93%	1.5 (0.71 to 3.0) 86%	2.1 (0.99 to 4.7) 97%	1.3 (0.65 to 2.7) 79%	--				
MTX+HCQ/CQ	8.9 (2.2 to 46) >99%	2.3 (0.55 to 13) 88%	2.2 (0.49 to 12) 85%	2.0 (0.48 to 11) 84%	0.74 (0.21 to 2.7) 30%	2.0 (0.43 to 11) 81%	2.5 (0.52 to 15) 88%	2.6 (0.60 to 14) 90%	2.5 (0.54 to 14) 89%	3.6 (0.73 to 21) 93%	2.2 (0.48 to 12) 83%	1.6 (0.38 to 9.3) 74%	--			
MTX+IMGold	16 (2.0 to 553) >99%	4.3 (0.51 to 146) 89%	3.9 (0.46 to 134) 87%	3.7 (0.44 to 129) 86%	1.3 (0.13 to 43) 57%	3.7 (0.40 to 124) 85%	4.6 (0.49 to 163) 89%	4.6 (0.57 to 166) 91%	4.5 (0.51 to 155) 90%	6.3 (0.71 to 234) 95%	3.9 (0.46 to 146) 87%	3.0 (0.34 to 107) 80%	1.9 (0.12 to 60) 65%	--		
MTX+LEF	5.7 (2.2 to 16) >99%	1.5 (0.56 to 4.5) 78%	1.4 (0.50 to 4.2) 73%	1.3 (0.48 to 3.8) 70%	0.46 (0.13 to 1.6) 11%	1.3 (0.40 to 4.2) 66%	1.6 (0.49 to 5.6) 78%	1.6 (0.60 to 5.0) 83%	1.6 (0.52 to 4.9) 80%	2.2 (0.71 to 7.5) 93%	1.4 (0.47 to 4.5) 72%	1.1 (0.36 to 3.3) 54%	0.64 (0.09 to 3.8) 30%	0.34 (0.01 to 3.7) 21%	--	
MTX+SSZ	2.5 (0.49 to 14) 87%	0.65 (0.12 to 3.6) 32%	0.60 (0.11 to 3.4) 29%	0.57 (0.11 to 3.2) 26%	0.21 (0.05 to 0.88) 2%	0.55 (0.10 to 3.2) 26%	0.70 (0.12 to 4.5) 36%	0.71 (0.14 to 4.1) 36%	0.69 (0.12 to 4.0) 34%	0.98 (0.17 to 6.1) 49%	0.61 (0.11 to 3.7) 30%	0.46 (0.08 to 2.7) 20%	0.28 (0.07 to 1.0) 3%	0.15 (0.00 to 2.4) 10%	0.46 (0.06 to 3.2) 20%	--
MTX+SSZ+HCQ	11 (4.5 to 31) >99%	2.8 (1.1 to 8.4) 99%	2.5 (0.97 to 8.0) 97%	2.4 (0.97 to 7.2) 97%	0.86 (0.53 to 1.4) 25%	2.3 (0.83 to 7.7) 95%	2.9 (0.98 to 10) 97%	3.0 (1.2 to 9.4) 99%	2.9 (1.1 to 9.2) 98%	4.1 (1.4 to 14) >99%	2.5 (0.93 to 8.5) 95%	1.9 (0.73 to 6.3) 90%	1.2 (0.35 to 3.7) 60%	0.66 (0.02 to 7.1) 39%	1.9 (0.49 to 7.7) 81%	4.1 (1.1 to 17) 98%

Treatment effects are presented as the median Odds Ratio (OR) with 95% credible intervals and the probability of superiority (higher odds of ACR50 response) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; AZA, azathioprine; CTZ, certolizumab; CQ, chloroquine; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C9. Treatment rankings for ACR50 response: MTX-inadequate response

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 17=worst) median (95%CrI)
MTX+IMGold	52.81	1 (1 to 15)
MTX+ETN	22.50	2 (1 to 5)
MTX+HCQ/CQ	14.14	4 (1 to 15)
MTX+SSZ+HCQ	6.28	3 (1 to 8)
MTX+LEF	3.39	6 (1 to 15)
MTX+TOFA	0.34	6 (2 to 13)
MTX+GOL (sc)	0.18	8 (3 to 15)
MTX+SSZ	0.14	15 (4 to 17)
MTX+GOL (IV)	0.11	12 (4 to 16)
MTX+ABAT (sc)	0.04	9 (5 to 15)
MTX+TCZ (8 mg/kg)	0.04	9 (4 to 15)
MTX+RTX	0.03	12 (5 to 16)
MTX	<0.01	17 (16 to 17)
MTX+ABAT (IV)	<0.01	11 (6 to 15)
MTX+ADA	<0.01	9 (5 to 13)
MTX+IFX	<0.01	12 (7 to 16)
MTX+TCZ (4 mg/kg)	<0.01	15 (8 to 16)

Abbreviations: ABAT, abatacept; ADA, adalimumab; AZA, azathioprine; CTZ, certolizumab; CQ, chloroquine; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C10. Pair-wise comparisons for radiographic progression (change from baseline, random-effects model): MTX-inadequate response

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	MTX+ETN	MTX+GOL (sc)	MTX+GOL (IV)	MTX+IFX
MTX+ABAT (IV)	-0.30 (-1.44 to 0.85) 84%	--						
MTX+ABAT (sc)	-0.48 (-2.03 to 1.2) 86%	-0.18 (-2.11 to 1.8) 67%	--					
MTX+ADA	-0.44 (-1.53 to 0.72) 90%	-0.14 (-1.71 to 1.5) 67%	0.04 (-1.11 to 1.2) 43%	--				
MTX+ETN	-0.60 (-2.41 to 1.2) 87%	-0.30 (-2.46 to 1.8) 72%	-0.11 (-2.59 to 2.3) 58%	-0.14 (-2.34 to 2.0) 61%	--			
MTX+GOL (sc)	-0.14 (-0.96 to 0.67) 76%	0.15 (-1.27 to 1.6) 32%	0.33 (-1.52 to 2.1) 21%	0.29 (-1.12 to 1.7) 19%	0.45 (-1.50 to 2.4) 20%	--		
MTX+GOL (IV)	-0.44 (-1.55 to 0.73) 89%	-0.15 (-1.76 to 1.5) 67%	0.04 (-1.99 to 2.0) 46%	0.00 (-1.62 to 1.5) 50%	0.15 (-1.98 to 2.3) 38%	-0.30 (-1.67 to 1.1) 80%	--	
MTX+IFX	-0.69 (-1.83 to 0.47) 94%	-0.40 (-2.04 to 1.2) 82%	-0.21 (-2.21 to 1.7) 67%	-0.24 (-1.89 to 1.3) 72%	-0.10 (-1.50 to 1.3) 62%	-0.55 (-1.97 to 0.88) 88%	-0.25 (-1.88 to 1.3) 73%	--
MTX+SSZ+HCQ	-0.41 (-2.02 to 1.2) 82%	-0.12 (-2.14 to 1.9) 60%	0.07 (-2.24 to 2.4) 45%	0.04 (-1.96 to 2.0) 47%	0.19 (-0.62 to 0.99) 18%	-0.27 (-2.11 to 1.5) 71%	0.03 (-1.95 to 2.0) 47%	0.28 (-0.85 to 1.4) 17%

Treatment effects are presented as the median standardized mean difference (smd) with 95% credible intervals and the probability of superiority (less radiographic progression) for the row versus column.

Abbreviations: ABAT, abatacept; ADA, adalimumab; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; sc, subcutaneous; SSZ, sulphasalazine

Table C11. Treatment rankings for radiographic progression (change from baseline, random-effects model): MTX-inadequate response

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 9=worst) median (95%CrI)
MTX+IFX	31.79	2 (1 to 7)
MTX+ETN	24.18	3 (1 to 9)
MTX+ABAT (sc)	17.41	4 (1 to 9)
MTX+GOL (IV)	10.96	4 (1 to 9)
MTX+ADA	6.17	4 (1 to 9)
MTX+ABAT (IV)	5.50	6 (1 to 9)
MTX+SSZ+HCQ	2.37	5 (2 to 9)
MTX+GOL (sc)	1.60	7 (2 to 9)
MTX	0.04	8 (4 to 9)

Abbreviations: ABAT, abatacept; ADA, adalimumab; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; sc, subcutaneous; SSZ, sulphasalazine

Table C12. Pair-wise comparisons for radiographic progression (change from baseline, fixed-effect model): MTX-inadequate response

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	MTX+ETN	MTX+GOL (sc)	MTX+GOL (IV)	MTX+IFX
MTX+ABAT (IV)	-0.29 (-0.49 to -0.09) >99%	--						
MTX+ABAT (sc)	-0.48 (-0.75 to -0.21) >99%	-0.18 (-0.53 to 0.15) 86%	--					
MTX+ADA	-0.44 (-0.66 to -0.23) >99%	-0.15 (-0.45 to 0.14) 84%	0.04 (-0.13 to 0.21) 34%	--				
MTX+ETN	-0.57 (-1.05 to -0.10) 99%	-0.28 (-0.81 to 0.23) 86%	-0.10 (-0.63 to 0.45) 63%	-0.13 (-0.65 to 0.39) 69%	--			
MTX+GOL (sc)	-0.13 (-0.34 to 0.07) 90%	0.16 (-0.13 to 0.45) 14%	0.35 (0.00 to 0.69) 2%	0.31 (0.01 to 0.60) 2%	0.44 (-0.07 to 0.96) 5%	--		
MTX+GOL (IV)	-0.44 (-0.64 to -0.24) >99%	-0.15 (-0.43 to 0.14) 84%	0.04 (-0.30 to 0.38) 41%	0.01 (-0.29 to 0.30) 48%	0.14 (-0.38 to 0.66) 31%	-0.30 (-0.59 to -0.02) 98%	--	
MTX+IFX	-0.68 (-1.03 to -0.34) >99%	-0.39 (-0.80 to 0.00) 97%	-0.21 (-0.65 to 0.23) 82%	-0.24 (-0.64 to 0.16) 88%	-0.11 (-0.44 to 0.21) 75%	-0.55 (-0.95 to -0.15) >99%	-0.25 (-0.66 to 0.15) 89%	--
MTX+SSZ+HCQ	-0.40 (-0.84 to 0.04) 96%	-0.10 (-0.60 to 0.38) 66%	0.08 (-0.43 to 0.60) 39%	0.04 (-0.43 to 0.53) 43%	0.17 (-0.01 to 0.36) 3%	-0.26 (-0.75 to 0.21) 86%	0.04 (-0.45 to 0.53) 44%	0.29 (0.02 to 0.56) 2%

Treatment effects are presented as the median standardized mean difference (smd) with 95% credible intervals and the probability of superiority (less radiographic progression) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IV, intravenous; MTX, methotrexate; sc, subcutaneous; SSZ, sulphasalazine

Table C13. Pair-wise comparisons for withdrawals due to adverse events: MTX-inadequate response

Medication	MTX	MTX+ABAT (IV)	MTX+ABAT (sc)	MTX+ADA	MTX+CTZ	MTX+ETN	MTX+GOL (sc)	MTX+GOL (IV)	MTX+IFX	MTX+RTX	MTX+TCZ (4 mg/kg)	MTX+TCZ (8 mg/kg)	MTX+TOFA	MTX+CyA	MTX+IMGold	MTX+LEF
MTX+ABAT (IV)	0.76 (0.44 to 1.3) 85%	--														
MTX+ABAT (sc)	0.55 (0.28 to 1.0) 97%	0.72 (0.42 to 1.3) 88%	--													
MTX+ADA	1.4 (0.95 to 2.3) 4%	1.9 (1.1 to 3.7) 1%	2.7 (1.4 to 4.9) <1%	--												
MTX+CTZ	1.4 (0.79 to 3.0) 13%	1.9 (0.85 to 4.7) 6%	2.6 (1.1 to 7.2) 2%	0.98 (0.47 to 2.3) 52%	--											
MTX+ETN	1.3 (0.56 to 3.0) 29%	1.6 (0.66 to 4.7) 17%	2.3 (0.83 to 6.8) 6%	0.87 (0.35 to 2.3) 61%	0.87 (0.30 to 2.6) 60%	--										
MTX+GOL (sc)	1.0 (0.39 to 2.8) 48%	1.4 (0.47 to 4.2) 31%	1.9 (0.63 to 6.0) 14%	0.70 (0.25 to 2.1) 72%	0.72 (0.21 to 2.3) 70%	0.81 (0.21 to 3.1) 62%	--									
MTX+GOL (IV)	1.3 (0.36 to 6.3) 34%	1.8 (0.42 to 9.4) 20%	2.4 (0.55 to 14) 11%	0.91 (0.22 to 5.0) 55%	0.92 (0.21 to 5.0) 54%	1.0 (0.24 to 5.7) 48%	1.3 (0.26 to 7.3) 37%	--								
MTX+IFX	1.6 (0.99 to 2.7) 3%	2.1 (1.1 to 4.6) 1%	3.0 (1.3 to 6.5) <1%	1.1 (0.59 to 2.1) 36%	1.1 (0.46 to 2.5) 39%	1.3 (0.56 to 3.0) 27%	1.6 (0.53 to 4.5) 21%	1.2 (0.24 to 5.3) 39%	--							
MTX+RTX	2.1 (0.74 to 6.4) 8%	2.8 (0.82 to 9.2) 5%	3.9 (1.1 to 13) 1%	1.5 (0.45 to 4.7) 25%	1.4 (0.40 to 5.5) 29%	1.7 (0.41 to 6.6) 24%	2.0 (0.50 to 8.6) 17%	1.6 (0.24 to 8.4) 28%	1.3 (0.41 to 4.3) 34%	--						
MTX+TCZ (4 mg/kg)	1.6 (0.95 to 2.9) 4%	2.2 (1.0 to 4.8) 2%	3.0 (1.3 to 7.0) 1%	1.1 (0.55 to 2.3) 37%	1.1 (0.47 to 2.7) 39%	1.3 (0.47 to 3.9) 32%	1.6 (0.54 to 4.7) 21%	1.2 (0.24 to 5.4) 39%	1.0 (0.47 to 2.1) 49%	0.78 (0.23 to 2.6) 65%	--					
MTX+TCZ (8 mg/kg)	1.7 (1.0 to 2.8) 2%	2.3 (1.0 to 4.8) 2%	3.1 (1.4 to 7.1) <1%	1.2 (0.60 to 2.3) 33%	1.2 (0.50 to 2.7) 35%	1.3 (0.50 to 3.7) 28%	1.7 (0.56 to 4.6) 19%	1.3 (0.25 to 5.5) 36%	1.1 (0.52 to 2.1) 44%	0.83 (0.23 to 2.5) 63%	1.0 (0.64 to 1.7) 42%	--				
MTX+TOFA	1.2 (0.74 to 2.3) 21%	1.6 (0.82 to 4.0) 9%	2.3 (1.1 to 5.4) 2%	0.86 (0.49 to 1.5) 70%	0.88 (0.35 to 2.0) 61%	0.99 (0.37 to 2.6) 51%	1.2 (0.40 to 4.2) 38%	0.96 (0.17 to 3.9) 52%	0.77 (0.37 to 1.7) 76%	0.59 (0.17 to 2.0) 80%	0.76 (0.34 to 1.9) 74%	0.73 (0.34 to 1.8) 78%	--			
MTX+CyA	3.3 (1.2 to 9.6) 1%	4.3 (1.4 to 15) 1%	6.0 (1.8 to 22) <1%	2.2 (0.73 to 7.5) 8%	2.3 (0.67 to 7.8) 10%	2.5 (0.68 to 10) 8%	3.2 (0.79 to 14) 6%	2.4 (0.37 to 14) 16%	2.0 (0.65 to 6.8) 12%	1.5 (0.35 to 6.8) 29%	2.0 (0.62 to 6.5) 12%	1.9 (0.61 to 6.1) 14%	2.6 (0.84 to 9.1) 5%	--		
MTX+IMGold	4.1 (0.49 to 103) 10%	5.6 (0.58 to 119) 7%	7.7 (0.81 to 173) 4%	2.8 (0.32 to 76) 18%	2.9 (0.32 to 70) 18%	3.4 (0.32 to 90) 17%	4.3 (0.39 to 93) 14%	3.2 (0.25 to 92) 19%	2.5 (0.27 to 72) 21%	2.0 (0.16 to 58) 30%	2.6 (0.26 to 68) 22%	2.5 (0.26 to 63) 24%	3.3 (0.39 to 91) 15%	1.3 (0.12 to 36) 42%	--	
MTX+LEF	1.9 (0.74 to 4.7) 8%	2.5 (0.87 to 7.3) 4%	3.4 (1.1 to 11) 1%	1.3 (0.46 to 3.6) 30%	1.3 (0.43 to 3.9) 33%	1.5 (0.41 to 5.2) 27%	1.8 (0.48 to 6.8) 19%	1.4 (0.22 to 6.8) 32%	1.1 (0.41 to 3.3) 39%	0.88 (0.22 to 3.6) 58%	1.1 (0.40 to 3.4) 40%	1.1 (0.39 to 3.2) 43%	1.5 (0.51 to 4.4) 23%	0.57 (0.13 to 2.3) 79%	0.46 (0.02 to 4.3) 74%	--
MTX+SSZ+HCQ	1.8 (0.87 to 3.9) 5%	2.4 (1.0 to 6.3) 2%	3.3 (1.3 to 9.3) 1%	1.3 (0.54 to 3.0) 30%	1.3 (0.43 to 3.3) 32%	1.4 (0.78 to 2.8) 14%	1.8 (0.52 to 6.1) 20%	1.4 (0.24 to 6.3) 34%	1.1 (0.57 to 2.2) 38%	0.86 (0.23 to 3.3) 59%	1.1 (0.45 to 2.9) 42%	1.1 (0.44 to 2.6) 45%	1.5 (0.59 to 3.7) 21%	0.57 (0.14 to 2.0) 80%	0.44 (0.02 to 4.5) 74%	0.98 (0.30 to 3.2) 51%

Treatment effects are presented as the median Rate Ratio (RR) with 95% credible intervals and the probability of superiority (lower odds of withdrawal) for the row versus column. Shaded cells reflect comparisons in which the credible interval excluded the null value.

Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Table C14. Treatment rankings for withdrawals due to adverse events: MTX-inadequate response

Intervention	Probability that treatment is best (%)	Average ranking (1=best, 17=worst) median (95%CrI)
MTX+ABAT (sc)	64.75	1 (1 to 5)
MTX+GOL (sc)	10.53	5 (1 to 15)
MTX+GOL (IV)	9.03	8 (1 to 17)
MTX+ABAT (IV)	6.85	3 (1 to 7)
MTX+ETN	3.18	7 (1 to 15)
MTX+IMGold	2.87	16 (1 to 17)
MTX+RTX	0.77	13 (3 to 17)
MTX+LEF	0.61	12 (3 to 17)
MTX+TOFA	0.43	7 (2 to 15)
MTX+CTZ	0.38	9 (3 to 16)
MTX	0.28	5 (2 to 8)
MTX+SSZ+HCQ	0.18	12 (4 to 17)
MTX+TCZ (4 mg/kg)	0.06	11 (4 to 16)
MTX+CyA	0.04	16 (7 to 17)
MTX+TCZ (8 mg/kg)	0.03	11 (5 to 16)
MTX+IFX	0.01	11 (5 to 15)
MTX+ADA	0	9 (4 to 15)

Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CyA, cyclosporine A; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

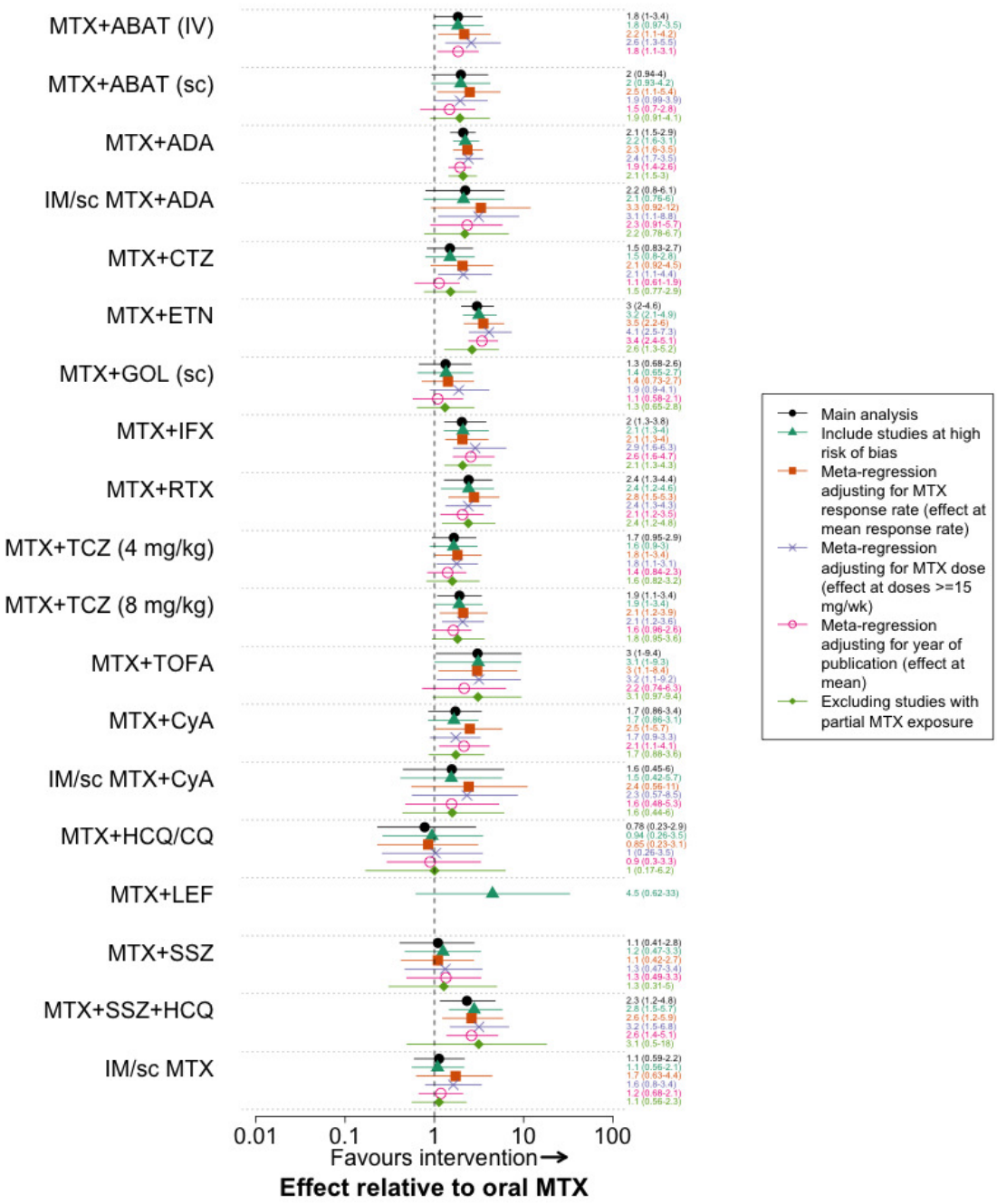
Sensitivity analyses for ACR50 response

Table C15. Meta-regression for ACR50 response

			MODEL FIT					
	Beta coefficient, median (CrI)	Interpretation	Unadjusted analysis			Adjusted analysis		
			DIC	Between-study standard deviation	Total residual deviance (number of parameters)	DIC	Between-study standard deviation	Total residual deviance (number of parameters)
MTX-naïve								
MTX response rate	-1.7 (-4.3 to 1.3)	Decrease in OR of 0.85 times (0.65 to 1.14) for every 10% increase in the response rate for MTX	609.2	0.19	64.8 (64)	610.9	0.21	64.6 (64)
Disease duration (years)	0.008 (-0.08 to 0.12)	Increase in OR of 1.01 times (0.92 to 1.12) for every year of disease duration	585.1	0.21	61.5 (62)	585.3	0.25	61.0 (62)
Duration of trial (weeks)	-0.002 (-0.01 to 0.007)	Decrease in OR of 0.97 times (0.87 to 1.1) for every 12 weeks of trial duration	609.2	0.19	64.8 (64)	609.2	0.23	63.6 (64)
MTX dose >= 15 mg/week	-0.34 (-0.80 to 0.03)	Decrease in OR of 0.71 times (0.45 to 1.0) for trials where the dose of MTX is >= 15 mg/wk	609.2	0.19	64.8 (64)	606.9	0.17	63.6 (64)
Year of publication of trial	0.049 (0.008 to 0.10)	Increase in OR of 1.05 times (1.01 to 1.11) for each year later of publication (range of years 2000-2015)	609.2	0.19	64.8 (64)	605.4	0.13	61.2 (64)
Swollen joint count	-0.04 (-0.12 to 0.03)	Decrease in OR of 0.96 times (0.89 to 1.03) for every 1 additional swollen joint at baseline	396.8	0.30	40.4 (40)	396.4	0.23	40.3 (40)
DAS-28	0.57 (-0.29 to 1.6)	Increase in OR of 1.8 times (0.74 to 5.2) for every 1 additional point increase in DAS28 at baseline	407.1	0.13	38.9 (40)	407.6	0.12	38.2 (40)
MTX-inadequate response								
MTX response rate	-5.3 (-8.5 to -2.8)	Decrease in OR of 0.59 times (0.43 to 0.75) for every 10% increase in the response rate for MTX	818.9	0.24	104.7 (97)	825.3	0.24	105.1 (97)
Disease duration (years)	0.10 (0.02 to 0.19)	Increase in OR of 1.11 times (1.02 to 1.21) for every year of disease duration	740.4	0.27	91.9 (87)	736.7	0.21	91.1 (87)
Duration of trial (weeks)	0.001 (-0.02 to 0.02)	Increase in OR of 1.02 times (0.83 to 1.22) for every 12 weeks of trial duration	818.9	0.24	104.7 (97)	819.3	0.26	104.0 (97)
MTX dose >= 15 mg/week	-0.17 (-0.53 to 0.20)	Decrease in OR of 0.85 times (0.59 to 1.22) for trials where the dose of MTX is >= 15 mg/wk	818.9	0.24	104.7 (97)	818.3	0.27	102.4 (97)
Year of publication of trial	-0.03 (-0.08 to 0.01)	Decrease in OR of 0.97 times (0.93 to 1.01) for each year later of publication (range of years 2000-2015)	818.9	0.24	104.7 (97)	819.5	0.21	105.5 (97)
Swollen joint count	0.02 (-0.05 to 0.08)	Increase in OR of 1.02 times (0.95 to 1.09) for every 1 additional swollen joint at baseline	728.0	0.26	92.0 (87)	727.3	0.27	91.8 (87)
DAS-28	0.23 (-0.31 to 0.79)	Increase in OR of 1.26 times (0.73 to 2.20) for every 1 additional point increase in DAS28 at baseline	546.7	0.25	71.1 (64)	548.3	0.27	71.1 (64)

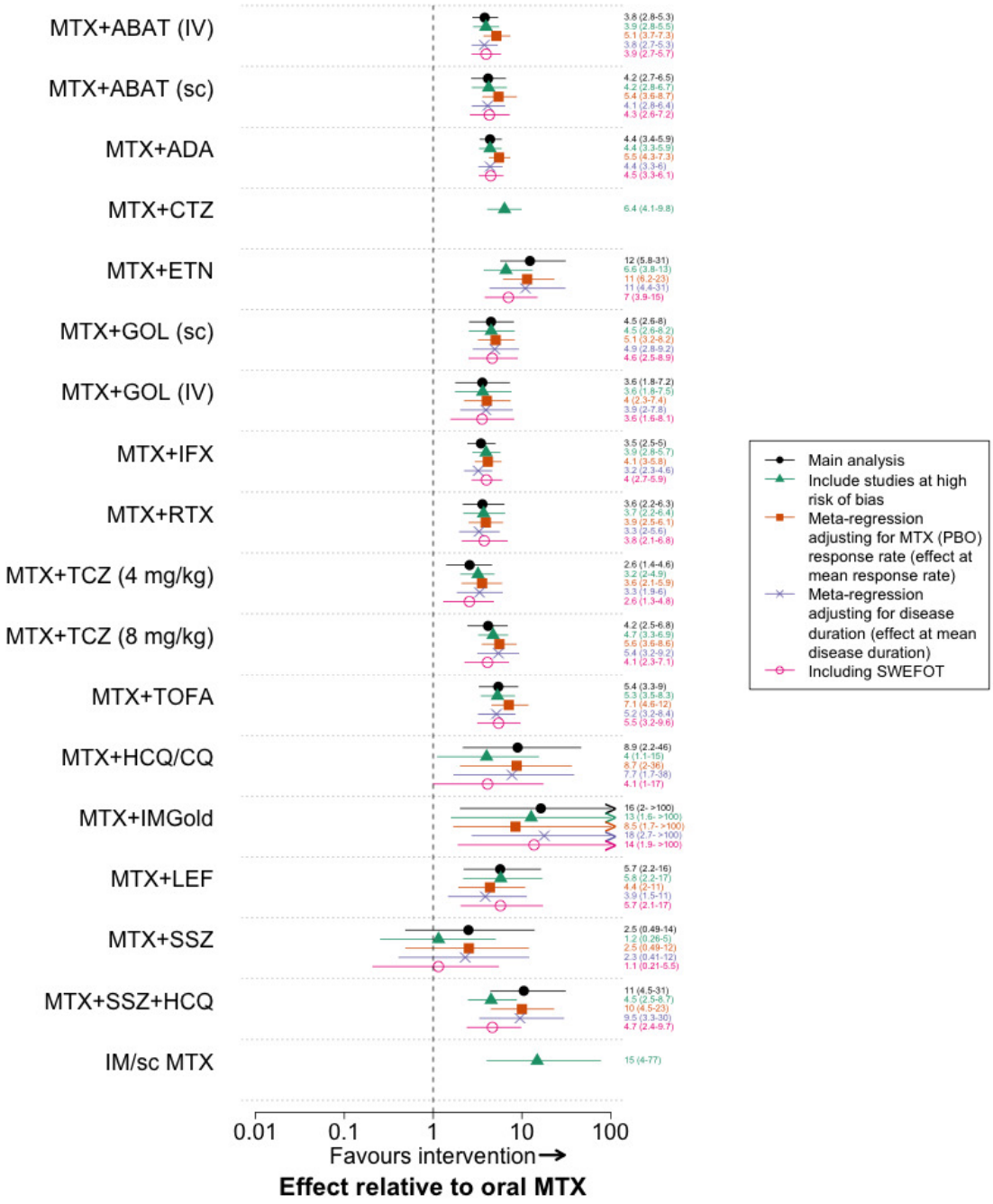
Abbreviations: CrI, credible interval; DIC, deviance information criterion; MTX, methotrexate; OR, odds ratio
Model fit between the unadjusted and adjusted analyses can be compared through the values for DIC, between study standard deviation and residual deviance (lower values means improved fit)

Figure C1. Selected meta-regression and sensitivity analyses for ACR50 response in MTX-naïve trials.



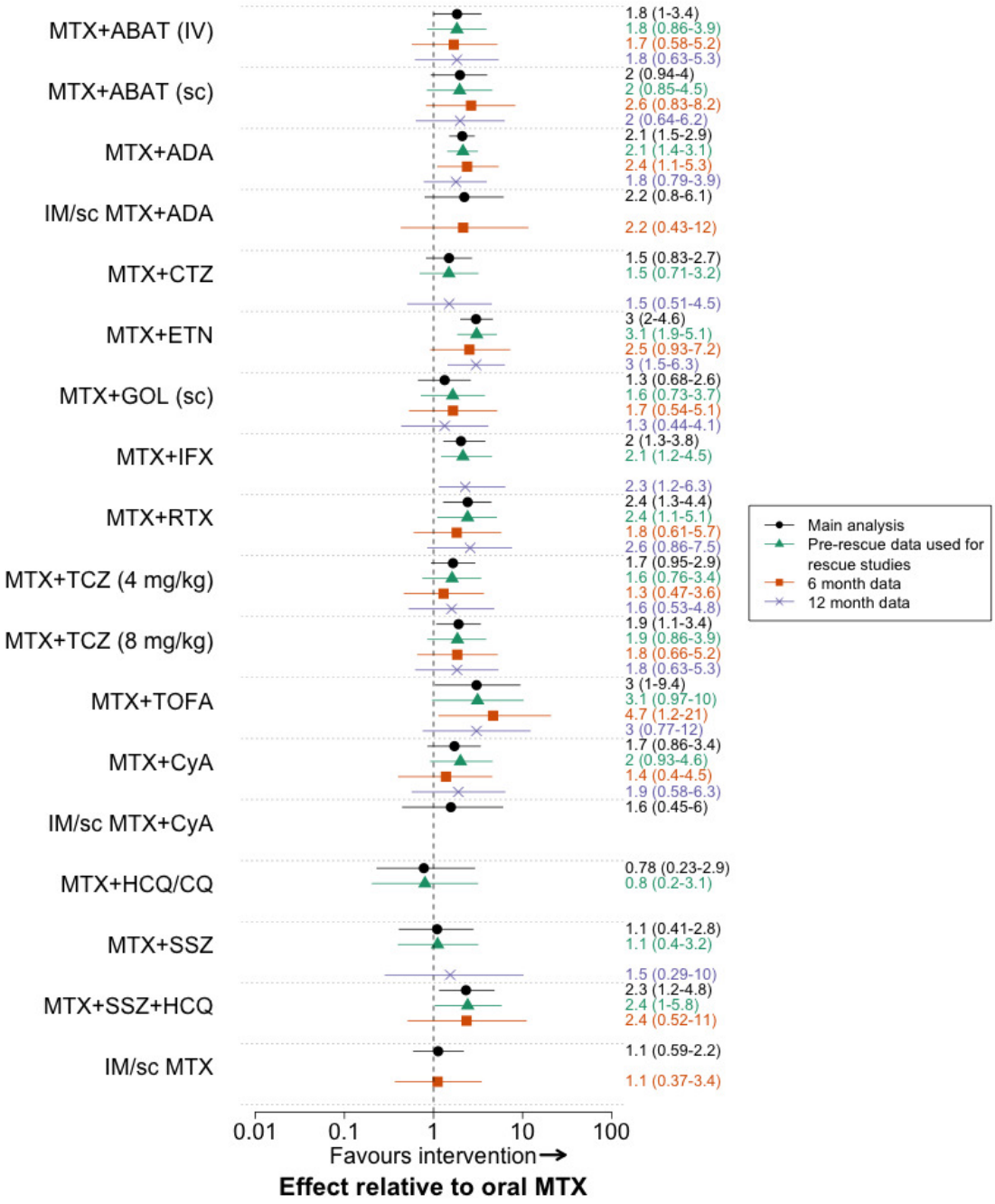
Abbreviations: ABAT, abatacept; ADA, adalimumab; CQ, chloroquine; CTZ, certolizumab; CyA, cyclosporine; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IM, intramuscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Figure C2. Selected meta-regression and sensitivity analyses for ACR50 response in MTX-inadequate response trials



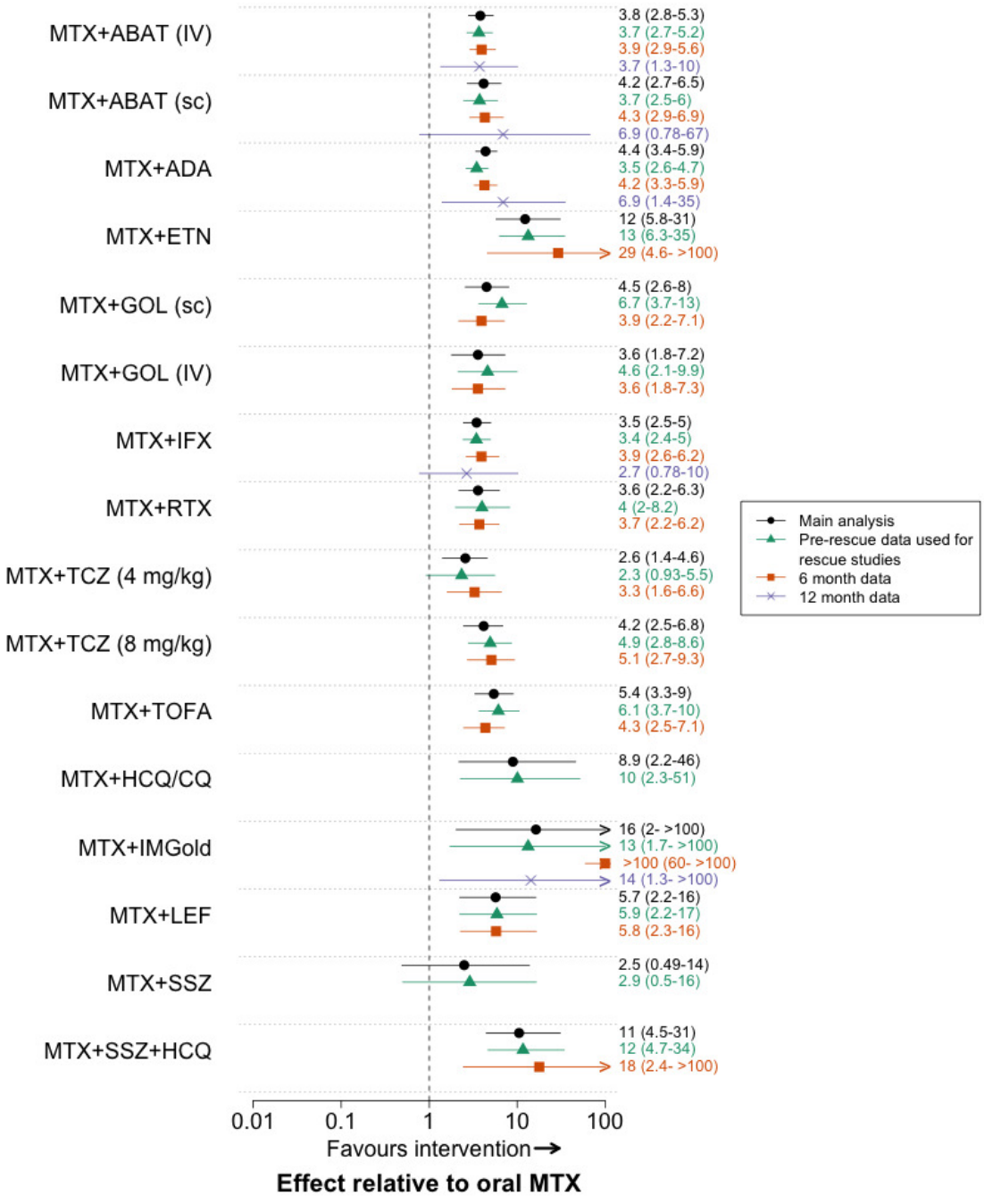
Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CQ, chloroquine; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IA, IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Figure C3. Sensitivity analyses for ACR50 response in MTX-naïve trials for different time-points of outcome assessment



Abbreviations: ABAT, abatacept; ADA, adalimumab; AZA, azathioprine; CQ, chloroquine; CTZ, certolizumab; CyA, cyclosporine; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IA, IM, intra-muscular; IV, intravenous; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib

Figure C4. Sensitivity analyses for ACR50 response in MTX-inadequate response trials for different time-points of outcome assessment



Abbreviations: ABAT, abatacept; ADA, adalimumab; CTZ, certolizumab; CQ, chloroquine; ETN, etanercept; GOL, golimumab; HCQ, hydroxychloroquine; IFX, infliximab; IA, IM, intra-muscular; IV, intravenous; LEF, leflunomide; MTX, methotrexate; RTX, rituximab; sc, subcutaneous; SSZ, sulphasalazine; TCZ, tocilizumab; TOFA, tofacitinib